UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/498,046	02/04/2000	Sabine Neirynck	VIB-08	8244

7590 07/21/2005

James F. Haley Jr.
Fish & Neave
1251 Avenue of the Americas
New York, NY 10020-1104

EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/498,046	NEIRYNCK ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-32,34 and 36-57* is/are pending in the application.

4a) Of the above claim(s) *42-45 and 47-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-32, 34, 36-41, 46 and 52-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-32, 34, 36-41, 46, and 52-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Applicant points out that while Jegerlehner states that M2e-HBc may be inferior to viral preparations for yearly epidemics, Jegerlehner also states that the fusion protein may be useful during a pandemic.

Applicant's arguments and a review of the reference have been fully considered, but are found unpersuasive. As a pandemic has not occurred, this discussion provided by Jegerlehner is purely speculative. Jegerlehner conclude that the M2e-HBc fusion protein offers poor protection against influenza epidemics that occur annually. This conclusion is evidenced by the fact that the M2e-HBc fusion protein does not induce anti-M2 IgA antibodies, see the second paragraph of the second column on page 5604 and Figure 3C of Jegerlehner. The fusion construct does not induce any viral neutralizing antibodies. In addition, Jegerlehner demonstrate that mice immunized with inactivated influenza virus were protected against higher doses of influenza virus than those mice administered with M2eHBc, see Figures 2, 3, 6 and the discussion section.

Applicant points to the teachings of Mozdzanowska, which discusses immune responses generated against the ectodomains of M2 in mice.

A review of the reference has been fully considered, but is found unpersuasive for several reasons, in no particular order. While Mozdzanowska is able to induce an antibody response with a fusion protein comprising M2e linked to helper T cell determinants and an adjuvant, the claims encompass M2e linked to any heterologous carrier with and without an adjuvant. Since it is clearly evident from the data presented by Heinen and Jegerlehner that M2e-HBc does not induce an antibody response and offers poor protection, the skilled artisan would be unable to predict which carrier among the genus claimed would induce the desired immune response. In addition, Mozdzanowska makes it clear that while M2e-MAP is able to induce "resistance against influenza virus replication in the respiratory tract of mice" (emphasis added), it is unclear what immune response would be induced in humans, see the last paragraph on page 2625. This is especially evident since the immune response with M2e-MAP induced in one animal model (mice) is favorable, while the immune response induced with M2e-HBc exacerbates disease in another (pigs), see the teachings of Heinen et al. Moreover, while Mozdzanowska teach induction of an antibody response with M2e-MAP (but not virus-specific memory Tc cells, see Figure 5), the skilled artisan would be hesitant to administer M2e-MAP in humans because Heinen reason that exacerbation of disease upon administration of M2e-HBc is due to induction of antibodies against M2e, see the top of the second column on page 1857.

Finally, the teachings of Zharikova et al. (Journal of Virology. June, 2005; 79 (11): 6644-6654) appear particularly pertinent against the conclusions of Mozdzanowska. It is noted that the same Mozdzanowska is also a co-author in the Zharikova et al. paper, which is published

after the Mozdzanowska paper cited by applicant. Zharikova et al. teach that escape mutants emerge in vivo that are able to evade anti-M2e antibodies, see the abstract and "Biologic properties of the M2e mutants" on page 6649. In view of the emergence of escape mutants in the presence of M2e specific antibodies, the skilled artisan would be hesitant to induce an antibody response against M2e with the M2e-MAP of Mozdzanowska (cited by applicant) because the escape mutants that would emerge could easily spread throughout an influenza-susceptible population. In addition, Zharikova et al. conclude that M2e-specific immunity cannot prevent or treat influenza virus infection and cannot be a substitute for the currently licensed vaccines, see the last paragraph on page 6653.

Applicant argues that Chen is not applicable against the instant claims because Chen uses a plasmid encoding NB and does not use a protein, as required by the instant claims. Applicant also points to the teachings of Lui et al., which shows cross-protection against influenza B with anti-M2e antibodies.

Applicant's arguments and a review of the reference have been fully considered, but are found unpersuasive. Although Chen uses a plasmid encoding NB, Chen is the only reference found in the prior art that attempts to use NB as a vaccine against influenza B. Chen clearly shows that NB fails to provide protection against influenza virus B, see the abstract and Table 2. The instant claims require a fusion protein comprising the extracellular portion of (a) M2, (b) NB or (c) CM2 and a heterologous carrier. However, there is no evidence present in the disclosure that supports the assertions of the claims that NB or CM2 ameliorate or prevent influenza virus infection. Since there is no guidance or working examples drawn to using NB or CM2 as a vaccine in the specification, the skilled artisan would be forced to consider teachings in the art

regarding the use of these proteins and their efficacy in vaccine compositions. As discussed, Chen clearly teaches that NB is ineffective against influenza B infections and there is no prior art that discusses the merits of using CM2 in an influenza vaccine composition (for which applicant offers no rebuttal). Therefore, it is maintained that the skilled artisan would doubt the efficacy of a vaccine comprising NB in view of the teachings of Chen. In addition the skilled artisan would reason that since the art demonstrates that the short, conserved peptides of influenza virus A and B are not efficacious as vaccines (as taught by Heinen et al., Jegerlehner et al., Zharikova et al. and Chen et al.), it is determined that the skilled artisan would doubt that the corresponding peptide present in the influenza C virus would be effective as a vaccine. Lui et al. do not discuss the use of NB or CM2. Therefore, Lui et al. do not remedy the lack of teaching in the art regarding the use of CM2 as a vaccine component, the lack of protective efficacy with NB or the lack of guidance provided in the specification with respect to using either of these proteins in a vaccine composition.

It is noted that applicant does not offer a rebuttal or even mention the teachings of Heinen et al. in this response. The teachings in the reference are still applicable against the instant claims and the rejections are maintained for reasons of record.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

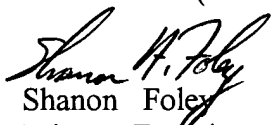
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 6:00 AM - 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Shanon Foley
Primary Examiner
Art Unit 1648